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TITLE: Feasibility Study and Demonstration Project for Joint Military/Civilian Trauma Institute with a Burn Center

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| 14. ABSTRACT The purpose of this grant was to continue to work collaboratively with partner organizations and advance the goals of patient care, research, and education. Goals include: to improve survival rates of military and civilian casualties, increase innovation in combat casualty care, improve educational experience for surgical/critical care trainees, improve pre-hospital evaluation and resuscitation, and facilitate metabolic monitoring of critically injured. | | | | | |
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INTRODUCTION

The University of Texas Health Science Center at San Antonio (UTHSC) proposed to utilize \$1.814M in congressional funding to work collaboratively with Brooke Army Medical Center (BAMC) and the US Army Institute of Surgical Research, Wilford Hall Medical Center (WHMC) and University Hospital (UH). The awarded grant enabled these partners to create the Trauma Institute of San Antonio, Texas (TRISAT), to conduct a financial and legal feasibility study and to demonstrate the capabilities of this joint military/civilian Trauma Institute with a Burn Center. This original grant was modified and \$1.35M in congressional funding was provided and used to continue this collaborative work. The awarded grant enabled these partners to create the Trauma Institute of San Antonio, Texas (TRISAT), now named the National Trauma Institute. This name change reflects the change in mission, vision and scope from a local effort to a more national effort. NTI became incorporated and recognized by the Internal Revenue Service as exempt from Federal income tax and exempt under section 501©(3) and further classified as a public charity. This change was made to allow NTI to apply for and administer grant funds directly as well as receive public donations to support national trauma research. This collaborative project has supported all partners to take advantage of their individual strengths in the areas of patient care, research and teaching and create a joint operation that is thought to have stronger sustainability. This successful partnership and work effort has given rise to the National Trauma Institute, positioned to increase and improve survival and quality of life for victims of trauma and burn injury. Funding and developing a national research agenda for trauma is critical to the health of our children and our troops.

[Administrative note: This original grant and subsequent modification have given rise to a subsequent proposal and contract. Studies included in this final report were begun through this funding and are continued under a separate contract (W81XWH-07-1-0717/STEWART) therefore, there is an overlap of progress for the two contracts. In addition, the funding for this grant was completed in April 2008. Progress is reported through the ending date of 25 October 2008 as requested. It was confirmed by the Project Officer that this report is to include the modified SOW only.]

Body:

The Modified Statement of Work includes these tasks which are addressed in detail in this section:

Research:

1. Establish procedures to identify upon admission to the emergency department those patients who may require a blood transfusion to employ the assessment of coagulation status of patients with traumatic injuries.
2. Implement programs and procedures to improve patient monitoring from the point of injury through the ICU. This will include implementation of decision assist paradigms and predictive models.
3. Implement programs and procedures to facilitate metabolic monitoring of the critically injured patient (trauma and burn). This effort will include development and implementation of standard care guidelines, point of care testing and decision assist programs.
4. Initiate an expansion of the program by providing epidemiological and statistical support to the identify differences between civilian and military patient populations and provide assessments as to the standard of care in relation to patient outcomes. This work will employ databases such as the National Trauma Data Base, TIRSAT Trauma Data Base, and the Joint Theater Trauma Registry.

Education:

15. Expand the educational aspect of the program by providing seed funding for resident research projects that foster collaboration between UTHSC, BAMC and WHMC. The intent of this effort is to obtain preliminary data to facilitate funding from other sources.

Research:

During the five years of this grant TRISAT has twice met the federal “exception from informed consent” requirements to obtain community consent in lieu of individual informed consent for clinical research. The first was for study of an artificial hemoglobin product developed by Northfield Laboratories and the second was for a study of low-dose Vasopressin, funded by the Office of Naval Research. The study: Prospective, Randomized, Double Blind, Multi Center Trial of Low Dose Vasopressin vs placebo in Traumatic Shock Resuscitation, PI Dr. Stephen Cohn, MD, Contract # W81XWH-08-1-0013 has been mentioned in the quarterly reports as an example of how the civilian and military hospitals are working together to further research.

TRISAT applied for NIH grants, sponsored studies, and grants from other agencies. Presently, one TRISAT member/physician serves as Principal Investigator on each grant/study and receives and disburses funds accordingly.

During the course of this grant, the focus of resuscitation studies was changed from assessing coagulation status to transfusion practices. The coagulation assessments are being performed at all three facilities, but are done under standard of care protocols, not research protocols and were not funded by this grant.

Resuscitation studies (hemorrhage control, coagulopathy, and damage control resuscitation):

| | Project | PI | Central Site | Add'l Sites | HRPO Approval# & Approval Date | Study exp. | Local IRB initial approval |
|---|---|---------------|--------------|-------------|---|------------|---------------------------------------|
| A | Multi-Center Retrospective Analysis of Transfusion Practices Correlated with Injury Severity and Outcomes in Trauma Patients (<i>Retro Review 30 centers Blood Transfusion Practices (part I DCR)</i>) | Holcomb, John | ISR | UT, et al | A-14257.a - .w 30 April 2007 - 20 November 2007 | 1.24.09 | <u>1/16/07 BAMC</u> 1/24/07 UT |

The Multi-Center Retrospective Review of Transfusion Practices (Damage Control Resuscitation) was initially approved by the Brooke Army Medical Center Institutional Review Board (BAMC IRB) on January 16, 2007. It has undergone a Continuing Review and was approved for continuation at the December 2008 BAMC IRB meeting. This initial retrospective chart reviews trauma patients receiving massive blood transfusions vs. patient who did not receive massive blood transfusions. Seventeen centers (including BAMC) have contributed data to this retrospective study. All data submitted has been included in the current data base and is part of the initial data analysis. All participating centers contributed data on all trauma patients that were admitted to their facilities between July 1, 2005 and June 30, 2006 and received at least one unit of packed red blood cells (PRBC) in the first 24 hours after admission; who met all other inclusion criteria and none of the exclusion criteria.

To house the data collected for this retrospective research study a web based data collection system was created by the Department of Epidemiology and Biostatistics at UTHSCSA and resides on a secure server. Data from the original 17 centers was migrated into this system in November 2007. Once migrated, data was then verified and system corrections were made. In February 2008, participating investigators were granted access to the system to view site specific data.

In addition to the 17 original participating centers, 7 other centers have joined this retrospective research study. Of those 7 centers, 2 have provided data to the lead site and that data has now become part of the total data set, 3 centers have sent data to the lead site and that data is in the process of being reviewed prior to incorporation into the overall data set, and the last two centers are in the data collection phase. The two centers collecting data have a suspense of July 15, 2008 for data submission. All regulatory correspondence and data will be forwarded to the lead site from these centers.

To date, a total of 16 proposals from participating investigators have been submitted for review to the study's Publication Committee and subsequently approved. Those proposals have been given to the consortium statistician for data acquisition and analysis in conjunction with the investigator/author submitting the proposal; for future publication and/or presentations. Currently five presentations and one publication have occurred utilizing the data collected for this study.

Proposals identified:

1. Dr Carrie Allison—Purpose: To evaluate whether female gender confers protection to traumatic insult, and specifically whether this group requires or receives fewer blood products compared to injury-matched men and post-menopausal females.
2. Dr John Holcomb—Title: Optimal plasma and platelet RBC ratios and center effect of our study
3. Dr John Holcomb—Title: Cause and Time to Death with Various Plasma:RBC Ratios in a Multi-Center Massive Transfusion Database
4. Dr John Holcomb—Title: Increased Platelet:RBC Ratios Are Associated With Improved Survival After Massive Transfusion
5. Dr Margaret Knudson-- Hypothesis: We hypothesize that patients receiving rFVIIa to control the coagulopathy associated with hemorrhage and acidosis following trauma will have a survival advantage when compared to similarly injured/metabolically deranged patients who did not receive this drug. We further hypothesize that we can identify which patients are most likely to benefit from rFVIIa and the proper timing of administration in relationship to other variables

such as pH, platelet count, temperature etc. We also predict that the complications potentially associated with the use of rFVIIa (DVT/PE/MI/arterial thrombosis) will be similar in both groups of patients.

6. Dr Rosemary Kozar—Title: OUTCOME IN PATIENTS WITH TRAUMATIC BRAIN INJURY REQUIRING MASSIVE TRANSFUSION AS A FUNCTION OF PLASMA AND PLATELET TRANSFUSION RATIOS
7. Dr David Shapiro—Title: Comparison of colloid type vs. crystalloid resuscitation. Are all colloids equal?
8. Dr Jason Sperry—Purpose: Purpose: We propose to characterize the independent risk of mortality associated with time to the OR after controlling for differences in resuscitation and transfusion practice. We intend to additionally see if the type of resuscitation and transfusion practice (FFP:PRBC ratio, Platelet:PRBC ratio, Use of aVIIa) a patient receives interacts and or moderates this time association.
9. Dr Philip Spinella—Title: The effectiveness and cost-effectiveness of different plasma and red blood cell transfusion ratios in massive transfusion for trauma
10. Dr Karen Zink—Purpose: To evaluate the ratio of blood products delivered in the first 6 hours after admission, to determine if that ratio made a difference in need for blood products or in overall mortality
11. Ronald Barbosa MD; Susan Rowell MD; Martin Schreiber MD—Hypothesis: Physiologic and biochemical data available to clinicians in the first 24 hours after presentation can be used to define cases in which ongoing massive transfusion is futile.
12. Susan Rowell MD, Ronald Barbosa MD—Hypothesis: The ratio response is different in blunt as compared to penetrating injury leading to a difference in the optimal ratio of fresh frozen plasma and platelets to packed red blood.
13. Dr Martin Schreiber, Dr Karen Zink—Purpose: Evaluate effect of gender on initial coagulation parameters and acid-base status following a traumatic injury.
14. Dr Martin Schreiber, Dr Karen Zink—Purpose: Evaluate effect of proportions of blood products on respiratory outcome
15. Dr Philip Spinella, Dr John Holcomb, and Dr Charles Wade—Title: rFVIIa and effect on mortality in DCR database
16. Karen Zink MD, Martin Schreiber MD—Hypothesis: Transfusion of FFP and platelets (PLT) is unnecessary and possibly harmful in patients who are not severely injured and only require 1-2 units of PRBCs, while patients requiring massive transfusion have a benefit with high ratios of FFP and PLT to PRBC. At some point, there is a threshold level of PRBC requirement where high ratios of these products lead to increased survival.

Publication: John B. Holcomb, MD, Charles E. Wade, PhD, Joel E. Michalek, PhD, Gary B. Chisholm, PhD. Lee Ann Zarzabal, MS, Martin A. Schreiber, MD, Ernest A. Gonzalez, MD, Gregory J. Pomper, MD, Jeremy G. Perkins, MD, Phillip C. Spinella, MD, Kari L. Williams, RN, and Myung S. Park, MD. *Increased Plasma and Platelet to Red Blood Cell Ratios Improves Outcome in 466 Massively Transfused Civilian Trauma Patients.* Ann Surg 2008; 248: 447–458

Publication Conclusion: Current transfusion practices and survival rates of massive transfusion (MT) patients vary widely among trauma centers. Conventional MT guidelines may underestimate the optimal plasma and platelet to RBC ratios. Survival in civilian MT patients is associated with increased plasma and platelet ratios. Massive transfusion practice guidelines should aim for a 1:1:1 ratio of plasma: platelets: RBCs.

An investigator meeting was held in June, 2007, to discuss results and future plans for further studies. A second investigator meeting was held in September 2007. At this meeting the data was presented and discussed. Specifics related to data granularity and data analysis were discussed. Sub-groups [Blood Banking, Research laboratories, Massive Transfusion Prediction Model, Publication Committee] presented issues/discussion. A prospective study was discussed at length to include type of study, end points, participating sites, data elements, clinical practice guidelines, and funding. A request for proposals for this prospective study was announced in May 2008 under a separate funding source.

Monitoring:

| | Project | PI | Central Site | Add'l Sites | HRPO Approval# & Approval Date | Study exp. | Local IRB initial approval |
|---|--|---------------|--------------|-------------|--|----------------------------------|----------------------------|
| B | Capture and Analysis of Prehospital Trauma VS enhanced Remote Triage and prediction of Life Saving Intervention (Prehospital VS study) | Salinas, Jose | ISR | UT | A-12859 This is the title of the proposal that was submitted for RAD funding. Currently covered under the Trauma Vitals protocol A-12859 | 11.17.08 (UT) 8..01.08 (BAMC) | 2/2/04 BAMC 1/27/05 UT |

B. Protocol Title: Capture and Analysis of Prehospital Trauma VS enhanced Remote Triage and prediction of Life Saving Intervention (Prehospital VS study)

PI: Jose Salinas, MD

This study was approved for implementation at UTHSCSA on 1/27/2005. BAMC IRB approval was obtained on 2/2/2004. This study underwent continuing review and was reapproved at UTHSCSA on 11/17/2007, as well as, BAMC reapproval on 8/1/2007. Data collection is ongoing.

Publication: Cancio, Leopoldo MD, Batchinsky, Andriy MD, Salinas, Jose PhD, Kuusela, Tom PhD, Convertino, Victor PhD, Wade, Charles PhD, and Holcomb, John MD. Heart-Rate Complexity for Prediction of Prehospital Lifesaving Interventions in Trauma Patients. *Journal of Trauma*. Vol 65:4 p 813-819.

Scientific conclusion: Decreased Heart rate complexity (HRC) is associated with Lifesaving interventions (LSI) in prehospital trauma patients. HRC may be useful as a new vital sign for identification of the severely injured. 800-beat sections of ECG data from prehospital trauma patients were analyzed by frequency-domain and complexity methods. Findings show that decreases in Sample Entropy and short-term correlations by Detrended Fluctuation Analysis, along with the motor component of the Glasgow Coma Scale score, were independently associated with the performance of LSIs. These “new vital signs” may improve clinical care by helping providers to identify those patients who need an LSI. Further work is needed to automate the waveform analysis process, and to decrease the number of ECGs rejected because of ectopy, noise, or short datasets.

Metabolic Monitoring studies: This task area includes several glucose control studies implemented at BMC/ISR, UHS/UTHSCSA, and institutions across the country. These studies are either ongoing, closed with ensuring data analysis, or protocols in draft. A national Symposium on Glucose control was held in July, 2007. Investigators from across the country participated in a two day discussion that reviewed findings in closed loop glucose control, share their experiences, and contribute to the development of a study protocol. This initial meeting was well attended and very successful in engendering collaboration nationally.

This table identifies the studies associated with this task area and their progress.

| | Project | PI | Central Site | Add'l Sites | HRPO Approval# & Approval Date | Study exp. | Local IRB initial approval |
|---|--|-------------------|--------------|-------------|--------------------------------|------------|----------------------------------|
| C | Continuous Glucose monitoring (CGM) versus Point of Care (POC) Glucometer in the ICU | Pidcoke, Heather | ISR | N/A | A-14364 | 7.11.09 | 8/3/06 BAMC 11/21/2006 UT* |
| D | Retrospective review of hyperglycemia and insulin therapy in patients with NSTI (January 1995- December 2005) AMENDMENT of additional dates Jan 2006- Dec 2007 | Pidcoke, Heather | UTHSC SA | N/A | A-14530.1 Approved 9.22.08 | 5.23.09 | 5/24/06 UT |
| E | A Retrospective Review of Point of Care versus Laboratory Glucose Values in the STICU | Corneille Michael | UTHSC SA | N/A | A-14530.2 Approved 9.22.08 | 6.2.09 | 6/2/08 UT |
| F | Retrospective Review of Variability in Blood Glucose as a predictor of Morbidity and Mortality in Patients with Traumatic Injuries (BAMC) | Pidcoke, Heather | BAMC | N/A | A-14365 Approved 11.7.07 | 10.26.08 | 4/27/2006 BAMC 10/26/2006 UT* |

| | | | | | | | |
|---|--|----------------------------------|------------|-----|--|---------|---|
| G | A Retrospective Review of Variability in Glucose as a Predictor of Morbidity and Mortality in Patients with Traumatic Injuries (includes diabetic subpopulation) UTHSCSA | Corneille Michael | UTHSC SA | N/A | A-14530.3 Approved 9.22.08 | 6.2.09 | 6/2/08 UT |
| H | Algorithmic adjustment to correct artificial elevation in point of care glucose measurement due to non-optimal hematocrit | Pidcoke, Heather | ISR | N/A | A-14363 Approved 11.7.07 | 1.5.08 | 3/1/06 BAMC 1/5/07 UT* |
| I | Animal Study The effect of insulin therapy on muscle atrophy and glycemic regulation in burned, hind limb unloaded rats (animal) | Wu, Xiaowu | ISR | N/A | ACURO Approved 4.18.08 | | BAMC/ISR IACUC 11/20/2007 |
| J | Retrospective Necrotizing Soft Tissue Registry Collaboration with UTHSC-Houston | Corneille Michael | UTHSC SA | N/A | | | Pending protocol submission (upon completion of #4 above-Retro review of hyperglycemia and insulin therapy in patients with NSTI) |
| K | Prospective Studies on Hyperglycemia in Surgical Infections | Corneille Michael | UTHSC SA | N/A | | | Pending protocol submission/site specific changes made. Present to UTHSCSA Faculty for approval to proceed. |
| L | Relationship Between Glucose and Cortisol Secretion in Critically Ill Burn/Trauma Patients: Impact of a Glycemic Control Protocol | Palmieri, Tina | UC Davis | N/A | Documents submitted for review 10.1.2008 | 7/7/09 | 7/7/08 |
| M | Modeling Glucose Variability in Critically Ill Trauma and Septic Surgical Patients | Kao, Lillian and Kozar, Rosemary | UT-Houston | N/A | Documents submitted for review 10.1.2008 | | PENDING APPROVAL Submitted to UTHSC-Houston IRB on 9/2008 |
| N | GlucoseScout Continuous Glucose Monitor versus Point of care in the STICU at UHS | Corneille Michael | UTHSC SA | N/A | | | Pending protocol development/site specific |
| O | Optimizing Blood Glucose Control in the Critically Ill | Gamelli Richard | Loyola | N/A | Documents submitted for review 10.1.2008 | 5/13/09 | Approved 5.13.2008 |
| P | Glucose Under the Curve: A Predictor of Morbidity and Mortality in ICU Patients | Corneille Michael | UTHSC SA | N/A | | | PENDING Approval |

* Study approval obtained due to PI being an employee of UTHSCSA and engaged in research at another facility.

Detailed information:

C. Protocol Title: Continuous Glucose monitoring (CGM) versus Point of Care (POC) Glucometer in the ICU

PI: Heather Pidcoke, MD (Study site: BAMC)

This protocol was originally approved at BAMC/ISR on 8/3/2006. The approved study site is BAMC. Continuing review was reapproved on 4/2/2008.

This study was approved at UTHSCSA (due to PI employer, UTHSCSA not study site) on 11/21/2006 and underwent continuing review and was approved for continuance on 6/20/2008.

An amendment to change the CGM device from the Guardian GT® due to the device requirement of accessible body surface area was submitted to the BAMC/ISR IRB on 7/3/2008. This amendment was made due to the fact that it was not feasible to use the Guardian RT® with the type of patients seen in the burn unit. After careful consideration, the PI and research team selected a new device for use. The new device is the GlucoScout VIA®. This device is the only FDA approved device for use in the critical care setting. Approval of this amendment was submitted on 7/3/08 and approval is pending.

This protocol will also be prepared for submission to the UTHSCSA IRB to be conducted at University Hospital upon BAMC/ISR IRB amendment approval with new device, GlucoScout VIA®.

Publication: Pidcock HF, Wolf SE, Holcomb JB, Wade CE. Subcutaneous continuous glucose monitoring (CGM) is accurate but imprecise in edematous trauma patients. Surgical Infection Society, *Surgical Infections*. 9: 221-237; 2008. (Abstract).

Pidcock HF, Wolf SE, Jones JA, Cohee BM, Holcomb JB, Wade CE. Diurnal pattern in endogenous insulin secretion persists in severely injured patients. Experimental Biology, *The FASEB Journal*. 22: 1205.7.

Presentation:

- The Surgical Infection Society. 28th Annual Meeting. 2008. Hilton Head, SC.
- Experimental Biology Annual Meeting, San Diego, 2008.
- Department of Defense Technologies for Metabolic Monitoring Program. Towards an Artificial Pancreas: An FDA/NIH/JDRF Workshop, session on “Beyond Insulin Dependent Diabetes,” Bethesda, MD. 2008. [included as attachment]
- Effect of Hematocrit Error in Point-of-Care Glucometers on Tight Glucose Control. Planning Committee for a Multi-Center Trial supported by the Juvenile Diabetes Research Foundation, the National Institutes of Health, and the Medical Research Materiel Command Session, Washington, DC. 2007.
- Advanced Technology Application for Combat Casualty Care. Annual Conference. St Pete Beach, FL. 2006.
- American Burn Association. 39th Annual Meeting. San Diego, CA. 2007.

D. Protocol Title: Retrospective review of hyperglycemia and insulin therapy in patients with NSTI

PI: Heather Pidcock, MD (Study site: UTHSCSA)

This study was originally approved on 5/22/2006. An amendment was submitted to UTHSCSA IRB on 4/29/2008 to include the addition of dates for study inclusion. The additional dates of January 2006 through December 2007 were approved by the UTHSCSA IRB on 5/5/08. In addition, this study underwent continuing review and was reapproved on 4/28/2008.

This study continues to be in the data collection phase. With the addition of 2 years, this has increased the number of patients screened and enrolled. The PI has streamlined the data collection process to reduce the total number of charts to be reviewed. Data collection continues to progress.

E. Protocol Title: A Retrospective Review of Point of Care versus Laboratory Glucose Values in the STICU

PI: Michael Corneille, MD (Study Site: UTHSCSA)

This study was approved by the UTHSCSA IRB on 6.2.2008. A database has been created and study personnel are in the process of querying medical records for subject screening and enrollment.

F. Protocol Title: Retrospective Review of Variability in Blood Glucose as a predictor of Morbidity and Mortality in Patients with Traumatic Injuries

PI: Heather Pidcoke, MD (Study site BAMC)

This study was approved at UTHSCSA with BAMC as the study site on 10/26/2006 (due to PI employer). BAMC/ISR approval received on 4/17/2006. This study underwent continuing review and was reapproved on 10/22/2007. This retrospective chart review continues with 300 patient charts reviewed and data collected. Data obtained from this study has been presented at:

- Society of Critical Care Medicine- Annual National Conference, Honolulu, HI, 2008
- Academic Surgical Congress-Annual Conference, Huntington Beach, CA, 2008.
- Western Trauma Conference-Annual National Conference, Steamboat Springs, CO, 2007.
- 59th Annual Southwestern Surgical Congress-Annual National Conference, Palm Springs, CA, 2007.
- Surgical Infection Society-Annual Conference. 27th Annual Meeting, Toronto, Canada. 2007.
- American College of Surgeons Clinical Congress Surgical Forum. 93rd Annual Clinical Congress Surgical Forum, New Orleans, LA. 2007.
- Academic Surgical Congress. 2nd Annual Academic Surgical Congress, Phoenix AZ. 2007.
- Society of Critical Care Medicine. 36th Critical Care Congress. Orlando, FL. 2007
- International Society of Burn Injury. 14th Congress. Fortaleza, Brazil. 2006.

Scientific conclusions: Diurnal patterns in blood glucose and insulin requirement mirror those of healthy subjects and may reflect persistence of normal variability in insulin activity. The 5-hour offset in peaks and troughs is suggestive of complex interplay between insulin availability and receptor sensitivity. The insulin requirement to blood glucose ratio increased, evidence that insulin resistance progresses over time.

Publication: Pidcoke, Heather, MD, Jose Salinas, PhD, Sandra Wanek, MD, Marybeth Concannon, BS, Florence Loo, BS, Kelly Wirfel, MD, John Holcomb, MD, Steven Wolf, MD and Charles Wade, PhD. “*Patterns of exogenous insulin requirements reflect insulin sensitivity changes in trauma.*” Critical Care Medicine, American Journal of Surgery 194 (2007) 798-803.

Pidcoke HF, Wade CE, Wanek SM, Wang JJ, Concannon M, Loo F, Wolf SE. Decreased mortality in burns with improved glucose control. Conference Proceedings for the 13th Congress International Society for Burn Injuries. (Abstract Peer-Reviewed).

Pidcoke HF, Wade CE, Wanek SM, Wang JJ, Concannon M, Loo F, Wolf SE. Critically injured patients demonstrate counter-regulatory mechanisms against hypoglycemia in the presence of intensive insulin therapy. Conference Proceedings of the Society for Critical Care Medicine in Critical Care Medicine. 34: A67. (Abstract Peer-Reviewed).

Pidcoke HF, Wanek SM, Salinas J, Holcomb JB, Concannon M, Loo F, Wolf SE, Wade CE. Chronobiology of glucose diurnal variation in critical injury re-established after disruption because of changes in time zone. Conference Proceedings of the American College of Surgeons Surgical Forum in the *Journal of the American College of Surgeons*. 205: S58-S58. (Abstract Peer-Reviewed).

Pidcoke HF, Rohleder LS, Wanek SM, Wang JJ, Holcomb JB, Wolf SE, Wade CE. Glucose variability is associated with high mortality after severe burn. Western Trauma Association, *The Journal of Trauma*. 62: 272. (Abstract Peer-Reviewed).

Pidcoke HF, Wade CE, Wanek SM, Salinas J, Holcomb JB, Concannon M, Loo F, Wolf SE. Diurnal variation in blood glucose in ICU burn patients. Academic Surgical Congress, *Journal of Surgical Research*. 137: 316-317; 2007. (Abstract Peer-Reviewed).

Pidcoke HF, Salinas J, Wanek SM, Concannon M, Loo F, Holcomb JB, Wolf SE, Wade CE. Glucose diurnal pattern is blunted in non-survivors versus survivors of burn injury. Academic Surgical Congress, *Journal of Surgical Research*. 144: 376. (Abstract Peer-Reviewed).

Pidcoke HF, Wanek SM, Wang JJ, Rohleder LS, Holcomb JB, Wolf SE, Wade CE. Glucose variability in the first week does not predict mortality. Surgical Infection Society, *Surgical Infections*. 8: 245-258. (Abstract Peer-Reviewed).

G. Protocol Title: A Retrospective Review of Variability in Glucose as a Predictor of Morbidity and Mortality in Patients with Traumatic Injuries (includes diabetic subpopulation)

PI: Michael Corneille, MD (Study site: UTHSCSA)

This study was approved by UTHSCSA IRB on 6/2/2008. University Hospital approval received on 6/26/2008. This retrospective study is in the beginning stages of data collection. Study personnel are in the process of querying medical records for data collection.

H. Protocol Title: Algorithmic adjustment to correct artificial elevation in point of care glucose measurement due to non-optimal hematocrit (Study site: BAMC)

PI: Heather Pidcoke, MD

This study was initially approved by BAMC/ISR on 3/1/2006 and UTHSCSA (due to PI employer) on 1/5/2007. This study underwent BAMC/ISR continuing review and was reapproved on 1/ 2/ 2008. UTHSCSA reapproval was given on 1/14/2008.

This study is still open to enrollment. An amendment was submitted to the BAMC/ISR IRB on 2/29/08 and approved on 3/4/08 with the addition of another 30,000 samples to the retrospective data set to allow evaluation of clinical impact of the correction formula, thereby providing tools to improve care for patients.

Scientific conclusion: A point-of-care (POC) glucometer (G1) used for critical care at BAMC/ISR is inaccurate in the presence of low hematocrit (HCT) values. The purpose of this study was to analyze error rates of three additional POC glucometer brands and determine mathematical correction formulas for each. Methods: Blood samples (n = 196) from a cohort of surgical, trauma, medical, cardiothoracic, and burn intensive care unit patients were tested on three commonly used POC glucometer brands (G2-G4). Results were compared with reference laboratory values, and correction compared with the validated formula for G1. A mathematical formula specific to each glucometer type was derived from glucose measurements, associated HCT values, and the degree of difference relative to laboratory results. Results: POC glucometer results were consistently elevated compared with reference laboratory values. Glucometer error rates for $HCT \leq 25\%$ ranged from 15.4% to 22.3% for the three types. Error rates for $25\% < HCT < 34\%$ ranged from 16.4% to 18.4%. A correction formula for each glucometer based on the natural log transformation of the HCT predicted reference values with a mean error rate of $-0.54\% \pm 5.6\%$ for G2, $-0.6\% \pm 5.5\%$ for G3, and $0.2\% \pm 8.0\%$ for G4. Correction was similar to that previously established for G1 ($-0.01\% \pm 4.8$). Conclusions: Significant error rates because of HCT effect were found in all glucometer models tested with accurate prediction of reference values with a simple mathematical formula.

Mann, Elizabeth A. RN, MS; Pidcoke, Heather F. MD; Salinas, Jose PhD; Holcomb, John B. MD; Wolf, Steven E. MD; Wade, Charles E. PhD. The Impact of Intensive Insulin Protocols and Restrictive Blood Transfusion Strategies on Glucose Measurement in American Burn Association (ABA) Verified Burn

Centers. *Journal of Burn Care & Research*. 29(5):718-723, September/October 2008.

Mann EA, Salinas J, Pidcock HF, Wolf SE, Holcomb JB, Wade CE. Error rates resulting from anemia can be corrected in multiple commonly used point-of-care glucometers. *Journal of Trauma*, Vol 64(1), January 2008, pp 15-21.

Mann EA, Pidcock HF, Salinas J, Wade CE, Holcomb JB, Wolf SE. Accuracy of glucometers should not be assumed. *Am J Crit Care*. 16: 531-2; 2007.

Pidcock HF, Wade CE, Mann EA, Salinas J, Michalek J, Cohee BM, Wolf SE. Occult hypoglycemia unmasked with an algorithm to correct hematocrit effect in point-of-care (POC) glucometers. American Burn Association, *The Journal of Burn Care & Research*. 28: S92. (Abstract Peer-Reviewed).

Pidcock HF, Wade CE, Mann EA, Salinas J, Jones JA, Cohee BM, Holcomb JB, Wolf SE. Correction of hematocrit effect in glucometers decreases hypoglycemia and improves moderate but not tight glucose control. The Society for Critical Care Medicine, *Critical Care Medicine*. 35: A64. (Abstract Peer-Reviewed).

I. Protocol Title: **Animal Study** The effect of insulin therapy on muscle atrophy and glycemic regulation in burned, hind limb unloaded rats (animal)

PI: Xiaowu Wu

This study was USA/ISR approved on 11/20/07 and will undergo continuing review on 11/20/08. Two animal studies for this project have been completed.

- 1). Glucose tolerance test in the rats of burn/hind limb (B/HU) unloading with or without continuous insulin treatment for 14 days.
- 2). Muscle and body composition change in the rats of burn/hind limb unloading with or without continuous insulin treatment for 14 days.

The results showed that daily insulin therapy improved weight loss, muscle atrophy and lipolysis induced by burn and hind limb unloading.

Insulin treatment improve glucose uptake, which was associated with reduction of body mass loss and disuse atrophy after burn and hind limb unloading.

Publications:

Pidcock HF, Wolf SE, Wu X, Baer LA, and Wade CE, Insulin Therapy Improves Glucose Disposal In Burned, Hind limb Unloaded Rats, 2008 International Shock Congress, Shock. 29:1-120.

Pidcock HF, Wu X, Baer LA, Wade CE, Wolf SE, The Effect of Insulin Therapy on Muscle Atrophy and Glycemic Regulation in Burned Hind limb Unloaded Rats (*Rattus norvegicus*), 2008 Conference Proceedings for the 14th Congress, International Society for Burn Injuries.

Presentations:

- The International Society for Burn Injury. 31st Annual Conference on Shock. Montreal Canada. 2008
- The International Shock Congress. 31st Annual Conference on Shock. Cologne, Germany. 2008.

J. Protocol Title: Retrospective Necrotizing Soft Tissue Infection Registry Collaboration with UTHSC-Houston.

PI: Michael Corneille, MD (Study site: UTHSCSA)

This is a multi-center retrospective collaboration. This protocol will be submitted to the UTHSCSA IRB upon completion of ongoing research project D listed on page 6) Titled: Retrospective review of hyperglycemia and insulin therapy in patients with NSTI (January 1995- December 2005) AMENDMENT of additional dates Jan 2006- Dec 2007. This study (item D, on page 7) captures at least the same data as this registry is seeking. Once project D is completed, an expedited protocol will be submitted to the UTHSCSA IRB to query the data needed from project D to complete this registry. This data will be maintained in a central repository located at UTHSC-Houston. Once all centers have contributed their data to this registry, participating PI's may use the data to answer research questions as they arise. This is particularly important given the rare occurrence of necrotizing infections and the barrier to systematic study. This collaboration will provide a greater set of data points and subjects from which the PI's can formulate research questions and increase the scientific strength of the study.

- K. Protocol Title: Prospective Studies on Hyperglycemia in Surgical Infections.
PI: Michael Corneille, MD (Study site: UTHSCSA)

This is a multi-center, prospective, consented, pilot research study. This study will enroll subjects from four participating centers:

- University Hospital (San Antonio)
- LBJ General Hospital (Houston)
- Ben Taub General Hospital (Houston)
- Methodist Hospital (Houston)

On August 4, 2008 Dr Lillian Kao (PI for UTHSC-Houston) and Dr Michael Corneille and their research coordinators met to discuss site specific modifications for this protocol. This protocol remains in editing phases. The hypothesis of this study is that strict glycemic control improves outcomes in patients with necrotizing soft tissue infections (NSTI) and proposes a mechanism by which this may occur. Upon completion of edits, this protocol will be submitted to the UTHSCSA IRB for approval and implementation.

- L. Protocol Title: Relationship between Glucose and Cortisol Secretion in Critically Ill Burn/Trauma Patients: Impact of a Glycemic Control Protocol.
PI: Tina Palmieri, MD (Study site: UC Davis)

This protocol was approved on 7/7/2008 by the IRB of University of California Davis. In addition, an amendment was submitted and approved to add study personnel to the protocol on 8/27/2008. This protocol was submitted to HRPO for review/approval on 10/1/08. A data management system has been created and research personnel are currently conducting chart reviews to populate the database based on study inclusion criteria. Sixty three records have been identified thus far for the first phase of the study and review of those charts remains in progress. Preliminary findings have allowed for submission of an abstract for the American Burn Association annual meeting.

- M. Protocol Title: Modeling Glucose Variability in Critically Ill Trauma and Septic Surgical Patients
PI: Lillian Kao, MD and Co-PI: Rosemary Kozar, MD (Study site: UTHSC-Houston)

The **overall hypothesis** of the study is that glucose variability can be mathematically modeled and that these models compare favorably to conventional statistical methods in predicting outcome in critically ill trauma and septic surgical patients. Ultimately, the research goal is to accurately perform early prediction of altered glucose variability in order to modify the aggressiveness of insulin therapy to modulate outcome. This protocol was submitted to the local IRB (UTHSCS-Houston) on 9/24/08. Local IRB approval is pending. This protocol was submitted to HRPO for review/approval on 10/1/08.

N. Protocol Title: GlucoScout Continuous Glucose Monitor versus Point of care in the STICU at UHS
PI: Michael Corneille, MD (study site: UTHSCSA)

This is a mirror image of the protocol in place at BAMC (Please refer to item 1 on page 5 of this document).

This protocol is undergoing modifications to meet site specific requirements to conduct this prospective trial at University Hospital. In addition, this protocol will be presented at the faculty research meeting at UTHSCSA prior to IRB submission to ensure the protocol meets all site specific requirements and investigators agree on methods/design. Upon completing this task, the protocol will be submitted to the UTHSCSA IRB for implementation. UTHSCSA researchers were awaiting the new device selection by BAMC researchers, which occurred on 7/3/2008. An amendment was submitted at that time to BAMC/ISR IRB. Approval is pending.

O. Protocol Title: Optimizing Blood Glucose Control in the Critically Ill
PI: Richard Gamelli, MD

This study was approved by Loyola IRB on 5/13/2008. The aim of this study is to conduct a retrospective review of patients admitted to the Foster G. McGaw Hospital Burn Center from 31 January 2003 to 1 April 2008, for the purpose of determining the association between serum glucose and variability patient outcomes. This protocol was submitted to HRPO for review/approval on 10/1/08. This study is in the process of screening all admitted patients (>2500) meeting inclusion criteria from medical records (2003-2007). Data management system selection is currently in progress.

P. Protocol Title: Glucose Under the Curve: A Predictor of Morbidity and Mortality in ICU Patients
PI: Michael Corneille, MD

This protocol is in the process of submission to UTHSCSA IRB. We hypothesize that area under the curve predicts outcome better than average daily glucose, single AM glucose, or time in the 80-110 mg/dL range in the ICU population.

Education

Resident/Fellow:

The Critical Care Consortium was established in the first year of this grant. The mission and vision for this group is to provide comprehensive training in all aspects of critical care while ensuring state of the art management of trauma, surgical, transplant and burn critical care patients. This is accomplished through a fully integrated consortium of anesthesia and surgical critical care staff at UTHSCSA, SAMMC-S, SAMMC-N, and the US Army Institute of Surgical Research that supports the clinical, research and teaching missions of the Trauma Institute of San Antonio (TRISAT).

Goals of the Fellowship: The Consortium develops and administers components of the integrated schedules and curriculum across the Critical Care Fellowship programs. The goals of the consortium include:

1. Develop world class surgical and anesthesia intensivists
2. Provide wide breadth of knowledge, teaching and clinical experience including across specialties to trainees
3. Provide cross spectrum of surgical, trauma, transplant and burn patients with critical illness
4. Foster an environment of mentorship not only for staff and fellows but between fellows and residents

5. Provide access to cutting edge medical and surgical practice for the diagnosis and management of patients with critical illness
6. Provide an environment to participate in and perform basic science, bench top, and clinical research

There have been three graduates each academic year since 2005/2006. Currently there are four Critical Care fellows for Academic Year 08-09 with one being a two year fellow in his second year. One fellow from Academic Year 07-08 is in his research year of the fellowship. The lecture series and reading compendium continue as an integral part of their education. In addition, a monthly journal club was added and the fellows agreed that this is a valuable addition. The lecture series and reading compendium were reviewed and revised to ensure the topics remain consistent with ACGME requirements without duplications. The lecture series is also attended by William Beaumont Army Medical Center in El Paso via video teleconference. Residents and fellows from the partner institutions remain involved in all aspects of research from design, implementation, analysis, and publication. The fellowship activities are supported by a website at UTHSC where the fellows complete evaluations and reading compendium self assessment questions.

[<http://surgery.uthscsa.edu/trisat/education.asp>]

Healthcare Team:

The Annual San Antonio Trauma Symposium has been a focus to provide education and research findings to the trauma health care team. Over the years, this multi-disciplinary conference has continued to focus on all aspects of trauma care from pre-hospital to critical care, surgical subspecialties, nursing, and rehabilitation. Attendance has been between 700 and 1000 each year. Plenary speakers over the years have included military and civilian experts in trauma care as well as policy makers and include: CAPT (Ret) Frank Butler, Col (Ret) Donald Jenkins, COL (Ret) John Holcomb, Dr. Basil A Pruitt, Jr, Mrs. Jorie Klein, Michael E. Kilpatrick – Deputy Director, Force Health Protection and Readiness Programs, DoD Health Affairs, MG Gale Pollock – Acting Surgeon General US Army, Dr. Donald Trunkey and Dr. Margaret Knudson, Dr. James Peake – Secretary Department of Veterans Affairs, Dr. Timothy Fabian – President American Association for Surgery of Trauma (AAST), Dr. S. Ward Casscells – Assistant Secretary of Defense for Health Affairs.

Other Opportunities for Collaboration

TRISAT coordinated the development of the Regional Trauma Registry and Database project with the state's Regional Advisory Council for Trauma. All of the hospitals providing trauma services in 22 counties, and 35 EMS companies participate by utilizing the same trauma registry software. This is resulting in available, accessible and standardized patient data for clinical research conducted by TRISAT and other qualified state and national health agencies.

NTI applied for and received a grant from the Texas Emerging Technology Fund. This grant focuses on technology associated with wireless vital sign monitoring.

Key Research Accomplishments

- Approval of federal exception from informed consent for Vasopressin Study
- Participation of 24 sites across the nation to participate in a retrospective study of transfusion practices
- Announcement of Prospective Massive Transfusion study based on data and experience of the Retrospective Transfusion Practice study.
- Expansion of metabolic monitoring studies including sites nationally.

Reportable Outcomes

- UTHSC applied for MRMC announcement number W81XHW-08-R-0013 based on their involvement in the Multi-Center Retrospective Review of Transfusion Practices (Damage Control Resuscitation)

Conclusion

This unique combination of military and civilian trauma and burn centers serves as a model of coordinated care, research and education. The research embarked on in this grant encompasses institutions across the country all with the goal of collaborative research partnerships to achieve the study enrollment numbers necessary for solid trauma research. The ongoing Multi-Center Retrospective Review of Transfusion Practices (Damage Control Resuscitation) significantly shaped the Prospective Massive Transfusion Coordinating Center announcement and will continue to serve as a strong basis for further studies. Both of these studies will serve to document the resuscitation patterns for trauma patients across the country and implement changes in clinical practice. The Metabolic Monitoring studies will enhance the knowledge of glucose control and metabolism of the critically ill and injured population as well as drive towards decision support in insulin delivery methods. Both of these research areas have broad implications in both the military and civilian community. The education component has grown in centers participating in the lecture series and attendance at the Trauma Symposium again affirming the focus in advancing trauma education for the entire healthcare team.